Complete Summary

GUIDELINE TITLE

Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services.

BIBLIOGRAPHIC SOURCE(S)

Smith DK, Grohskopf LA, Black RJ, Auerbach JD, Veronese F, Struble KA, Cheever L, Johnson M, Paxton LA, Onorato IM, Greenberg AE. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep 2005 Jan 21;54(RR-2):1-26. [126 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Management of possible sexual, injecting-drug-use, or other nonoccupational exposure to HIV, including considerations related to antiretroviral therapy. Public Health Service statement. Centers for Disease Control and Prevention. MMWR Recomm Rep 1998 Sep 25;47(RR-17):1-14.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- July 24, 2008, Ziagen (abacavir sulfate): The U.S. Food and Drug Administration (FDA) has notified the maker of abacavir and abacavir-containing medications of the need to add information to the current BOXED WARNING about the recommendation to test all patients for the HLA-B*5701 allele before starting or restarting therapy with abacavir or abacavir-containing medications.
- September 10, 2007, Viracept (nelfinavir mesylate): Pfizer issued a Dear Healthcare Professional Letter to inform healthcare professionals of the presence of ethyl methanesulfonate (EMS), a process-related impurity in Viracept and to provide guidance on the use of Viracept in pregnant women and pediatric patients.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

- Human immunodeficiency virus (HIV) infection
- Acquired immunodeficiency syndrome (AIDS)

GUIDELINE CATEGORY

Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Pediatrics
Preventive Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To summarize knowledge about the use and potential efficacy of nonoccupational postexposure prophylaxis (nPEP) and to detail guidelines for its use in the United States

TARGET POPULATION

Persons exposed to HIV through nonoccupational activities

In this report, a nonoccupational exposure is any direct mucosal, percutaneous, or intravenous contact with potentially infectious body fluids that occurs outside perinatal or occupational situations (e.g., health-care, sanitation, public safety, or laboratory employment). Potentially infectious body fluids are blood, semen, vaginal secretions, rectal secretions, breast milk, or other body fluid that is contaminated with visible blood.

INTERVENTIONS AND PRACTICES CONSIDERED

General Management

1. Consultation with infectious disease or human immunodeficiency virus (HIV)-care specialist
2. Facilitation of medication adherence
3. Follow-up testing and care
4. HIV prevention counseling
5. Management of source persons
6. Reporting and confidentiality

Laboratory Evaluations

1. Blood chemistry including, serum liver enzymes, blood urea nitrogen/creatinine, and complete blood count with differential
2. Pregnancy test (for women of reproductive age)
3. Sexually transmitted diseases screen (gonorrhea, chlamydia, syphilis) and hepatitis B and C serology
4. HIV antibody testing, HIV viral load (for source), HIV resistance testing (for source) and CD4+T lymphocyte count (for source)

Treatment

1. Use of starter pack for medications
2. Emergency contraception
3. Initiation of highly active antiretroviral therapy (HAART)

Antiretroviral Agents

1. Nucleoside and nucleotide reverse transcriptase inhibitors
    - Abacavir (Ziagen®, ABC)
    - Didanosine (Videx®, ddI)
    - Emtricitabine (Emtriva®, FTC)
    - Lamivudine (Epivir®, 3TC)
    - Stavudine (Zerit®, d4T)
    - Tenofovir (Viread®)
    - Zidovudine (Retrovir®, AZT)
2. Non-nucleoside reverse transcriptase inhibitors
    - Efavirenz (Sustiva®)
3. Protease inhibitors (PIs)
    - Atazanavir (Reyataz®)

- Fosamprenavir (Lexiva®)
- Indinavir (Crixivan®)
- Nelfinavir (Viracept®)
- Ritonavir (Norvir®)
- Saquinavir (hard-gel capsule) (Invirase®)
- Saquinavir (soft-gel capsule) (Fortovase®)

4. Combination tablets
    - Lopinavir/ritonavir (Kaletra®)
    - Zidovudine/lamivudine (Combivir®)
    - Zidovudine/lamivudine/abacavir (Trizivir®)
    - Lamivudine/abacavir (Epzicom®)
    - Emtricitabine/tenofovir (Truvada®)

Considerations for Special Groups

1. Pregnant women/women of childbearing potential
2. Children
3. Sexual assault survivors
4. Prison inmates
5. Injection drug users

MAJOR OUTCOMES CONSIDERED

- Prevention of human immunodeficiency virus (HIV) transmission
- Side effects and toxicity of antiretroviral agents
- Treatment adherence
- Behavior changes potentially related to prophylactic antiretroviral therapy
- Acquisition of antiretroviral-resistant HIV strains
- Cost of antiretroviral postexposure prophylaxis

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Cost-effectiveness of Nonoccupational Postexposure Prophylaxis (nPEP)

Although the potential benefits of nPEP to persons are measured by balancing its anticipated efficacy after a given exposure against individual health risks, the value of nPEP as a public health intervention is best addressed at the population level by using techniques such as cost-benefit analysis. Such analyses have been published. One cost-effectiveness evaluation of nPEP in different potential exposure scenarios in the United States reported it to be cost-effective only in situations in which the sex partner source was known to be human immunodeficiency virus (HIV)-infected or after unprotected receptive anal intercourse with a homosexual or bisexual man of unknown serostatus. A similar analysis in France reported that nPEP was cost-saving for unprotected receptive anal intercourse with a partner known to be HIV-infected and cost-effective for receptive anal intercourse with a homosexual or bisexual partner of unknown serostatus. It was not cost-effective for penile-vaginal sex, insertive anal intercourse, or other exposures considered.

Another study and anecdotal reports indicate difficulty limiting nPEP to the exposures most likely to benefit from it. In British Columbia, where guidelines for nPEP use have been implemented, an analysis indicated that >50% of those receiving nPEP should not, according to the guidelines, have been treated (e.g., for exposure to intact skin). The use of nPEP in these circumstances doubled the estimated cost per HIV infection prevented ($530,000 versus $230,000).

Even if nPEP is cost-effective for the highest risk exposures, behavioral interventions are more cost-effective. This emphasizes the importance, when considering nPEP, of providing risk-avoidance and risk-reduction counseling to reduce the occurrence of future HIV exposures.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations for Use of Antiretroviral nPEP

A 28-day course of highly active antiretroviral therapy (HAART) is recommended for persons who have had nonoccupational exposure to blood, genital secretions, or other potentially infected body fluids of persons known to be human immunodeficiency virus (HIV) infected when that exposure represents a substantial risk for HIV transmission (see algorithm for evaluation and treatment of possible nonoccupational HIV exposures [Figure 1] in the original guideline document) and when the person seeks care within 72 hours of exposure. When indicated, antiretroviral nonoccupational postexposure prophylaxis (nPEP) should be initiated promptly for the best chance of success.

Evidence from animal studies and human observational studies demonstrate that nPEP administered within 48 to 72 hours and continued for 28 days might reduce the risk for acquiring HIV infection after mucosal and other nonoccupational exposures. The sooner nPEP is administered after exposure, the more likely it is to interrupt transmission. Because HIV is an incurable transmissible infection that affects the quality and duration of life, HAART should be used to maximally suppress local viral replication that otherwise might occur in the days after exposure and potentially lead to a disseminated, established infection. One of the HAART combinations recommended for the treatment of persons with established HIV infection should be selected on the basis of adherence, toxicity, and cost considerations (see table below entitled "Antiretroviral Regimens for Nonoccupational Postexposure Prophylaxis of HIV Infection" and the table entitled "Highly Active Antiretroviral Therapy Medications, Adult Dosage, Cost, and Side Effects" [Table 3] in the original guideline document).

Antiretroviral Regimens for Nonoccupational Postexposure Prophylaxis of HIV Infection

Preferred regimens	
NNRTI[1]-based	Efavirenz[2] plus (lamivudine or emtricitabine) plus (zidovudine or tenofovir)
PI-based[1]	Lopinavir/ritonavir (co-formulated as Kaletra) plus (lamivudine or emtricitabine) plus zidovudine
Alternative regimens	

NNRTI-based	Efavirenz plus (lamivudine or emtricitabine) plus abacavir or didanosine or stavudine[3]
PI-based	Atazanavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or didanosine) or (tenofovir plus ritonavir [100 mg/day]) Fosamprenavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine) or (abacavir or tenofovir or didanosine) Fosamprenavir/ritonavir[4] plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine) Indinavir/ritonavir[4], [5] plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine) Lopinavir/ritonavir (co-formulated as Kaletra) plus (lamivudine or emtricitabine) plus (stavudine or abacavir or tenofovir or didanosine) Nelfinavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine) Saquinavir (hgc[1] or sgc[1])/ritonavir[4] plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
Triple NRTI[1]	Abacavir plus lamivudine plus zidovudine (only when an NNRTI- or PI-based regimen cannot or should not be used)

[1]NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; sgc = soft-gel saquinavir capsule (Fortovase); hgc = hard-gel saquinavir capsule (Invirase).
[2]Efavirenz should be avoided in pregnant women and women of childbearing potential.
[3]Higher incidence of lipoatrophy, hyperlipidemia, and mitochondrial toxicities associated with stavudine than with other NRTIs.
[4]Low-dose (100-400 mg) ritonavir. See Table 4 in the original guideline document for doses used with specific PIs.
[5]Use of ritonavir with indinavir might increase risk for renal adverse events.

Source: U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents, October 29, 2004 revision. Available at http://www.aidsinfo.nih.gov/guidelines/default_db2.asp?id=50. This document is updated periodically; refer to website for updated versions.

No evidence indicates that any specific antiretroviral medication or combination of medications is optimal for use as nPEP. However, on the basis of the degree of experience with individual agents in the treatment of HIV-infected persons, certain agents and combinations are preferred. Preferred regimens include efavirenz and lamivudine or emtricitabine with zidovudine or tenofovir (as a nonnucleoside-based regimen) and lopinavir/ritonavir (coformulated in one tablet as Kaletra®) and zidovudine with either lamivudine or emtricitabine. Different

alternative regimens are possible (see table above entitled "Antiretroviral Regimens for Nonoccupational Postexposure Prophylaxis of HIV Infection").

No evidence indicates that a three-drug HAART regimen is more likely to be effective than a two-drug regimen. The recommendation for a three-drug HAART regimen is based on the assumption that the maximal suppression of viral replication afforded by HAART (the goal in treating HIV-infected persons) will provide the best chance of preventing infection in a person who has been exposed. Clinicians and patients who are concerned about potential adherence and toxicity issues associated with a three-drug HAART regimen might consider the use of a two-drug regimen (i.e., a combination of two reverse transcriptase inhibitors). Regardless of the regimen chosen, the exposed person should be counseled about the potential associated side effects and adverse events that require immediate medical attention. The use of medications to treat symptoms (e.g., antiemetics or antimotility agents) might improve adherence in certain instances.

Although certain preliminary studies have evaluated the penetration of antiretroviral medications into genital tract secretions and tissues, evidence is insufficient to recommend a specific antiretroviral medication as most effective for nPEP. In addition, new antiretroviral medications might become available. As new medications and new information become available, these recommendations will be amended and updated.

When the source-person is available for interview, his or her history of antiretroviral medication use and most recent viral load measurement should be considered when selecting antiretroviral medications for nPEP. This information might help avoid prescribing antiretroviral medications to which the source-virus is likely to be resistant. If the source-person is willing, the clinician might consider drawing blood for viral load and resistance testing, the results of which might be useful in modifying the initial nPEP medications if the result scan be obtained promptly.

For persons who have had nonoccupational exposure to potentially infected body fluids of a person of unknown HIV infection status, when that exposure represents a substantial risk for HIV transmission (see algorithm for evaluation and treatment of possible nonoccupational HIV exposures [Figure 1] in the original guideline document) and when care is sought within 72 hours of exposure, no recommendations are made either for or against the use of antiretroviral nPEP. Clinicians should evaluate the risk for and benefits of this intervention on a case-by-case basis.

When a source-person is not known to be infected with HIV, the risk for exposure (and therefore the potential benefit of nPEP) is unknown. Prescribing antiretroviral medication in these cases might subject patients to risks that are not balanced with the potential benefit of preventing the acquisition of HIV infection. Judging whether the balance is appropriate depends entirely on the circumstances of the possible exposure (i.e., the risk that the source is HIV infected and the risk for transmission if the source is HIV infected) and is best determined through discussion between the clinician and the patient.

If the source-person is available for interview, additional information about risk history can be obtained and permission for an HIV test requested to assist in determining the likelihood of HIV exposure. When available, Food and Drug Administration (FDA)-approved rapid HIV tests are preferable for obtaining this information as quickly as possible. These additional factors might assist in the decision whether to start or complete a course of nPEP. If data to clearly determine risk are not immediately available, clinicians might consider initiating nPEP while further assessments are being made and then stopping it when other information is available (e.g., the source-person is determined to be noninfected).

For persons whose exposure histories represent no substantial risk for HIV transmission (see algorithm for evaluation and treatment of possible nonoccupational HIV exposures [Figure 1] in the original guideline document) or who seek care >72 hours after potential nonoccupational HIV exposure, the use of antiretroviral nPEP is not recommended. When the risk for HIV transmission is negligible, limited benefit is anticipated from the use of nPEP. In addition, animal and human study data demonstrate that nPEP is less likely to prevent HIV transmission when initiated >72 hours after exposure. Because the risks associated with antiretroviral medications are likely to outweigh the potential benefit of nPEP in these circumstances, nPEP is not recommended for such exposures, regardless of the HIV status of the source. However, it cannot be concluded on the basis of the available data that nPEP will be completely ineffective when initiated >72 hours after exposure. Moreover, data do not indicate an absolute time after exposure beyond which nPEP will not be effective. When safer and more tolerable drugs are used, the risk-benefit ratio of providing nPEP >72 hours postexposure is more favorable. Therefore, clinicians might consider prescribing nPEP after exposures that confer a serious risk for transmission, even if the exposed person seeks care >72 hours post exposure if, in the clinician's judgment, the diminished potential benefit of nPEP outweighs the potential risk for adverse events from antiretroviral drugs.

Considerations for All Patients Treated with Antiretroviral nPEP

Use of Starter Packs

Patients might be under considerable emotional stress when seeking care after a potential HIV exposure and might not attend to, or retain, all the information relevant to making a decision about nPEP. Clinicians should give an initial prescription for 3 to 5 days of medication and schedule a follow-up visit to review the results of baseline HIV testing (if rapid tests are not used), provide additional counseling and support, assess medication side effects and adherence, and provide additional medication if appropriate (with an altered regimen if indicated by side effects or laboratory test results).

Scientific Consultation

When clinicians are not experienced with using HAART or when information from source-persons indicates the possibility of antiretroviral resistance, consultation with infectious disease or other HIV-care specialists, if it is available immediately, might be warranted before prescribing nPEP. Similarly, when considering prescribing nPEP to pregnant women or children, consultation with obstetricians or pediatricians might be advisable. However, if such consultation is not immediately

available, initiation of nPEP should not be delayed. An initial nPEP regimen should be started and, if necessary, revised after consultation is obtained. Patients who seek nPEP might benefit from referral for psychological counseling that helps ease the anxiety about possible HIV exposure, strengthens risk-reduction behaviors, and promotes adherence to nPEP regimens if prescribed.

Facilitating Adherence

Adherence to antiretroviral medications can be challenging, even for 28 days. In addition to common side effects such as nausea and fatigue, each dose reminds the patient of his or her risk for acquiring HIV infection. Adherence has been reported to be especially poor among sexual assault survivors. Steps to maximize medication adherence include prescribing medications with fewer doses and fewer pills per dose, educating patients about the importance of adherence and about potential side effects, offering ancillary medications for side effects (e.g., anti-emetics) if they occur, and providing access to ongoing encouragement and consultation by phone or office visit.

Follow-up Testing and Care

All patients seeking care after HIV exposure should be tested for the presence of HIV antibodies at baseline and at 4 to 6 weeks, 3 months, and 6 months after exposure to determine whether HIV infection has occurred. In addition, testing for sexually transmitted diseases, hepatitis B and C, and pregnancy should be offered (see Table 4 in the original guideline document).

Patients should be instructed about the signs and symptoms associated with acute retroviral infection (see Table 5 in the original guideline document), especially fever and rash, and asked to return for evaluation if these occur during or after nPEP. Acute HIV infection is associated with high viral loads. However, clinicians should be aware that available assays might yield low viral-load results (e.g., <3,000) in noninfected persons. Such false positive results can lead to misdiagnosis of HIV infection.

Transient, low-grade viremia has been observed both in macaques exposed to simian immunodeficiency virus (SIV) and humans exposed to HIV who were administered antiretroviral PEP and did not become infected. In certain cases, this outcome might represent aborted infection rather than false-positive test results, but this can be determined only through further study. For patients with clinical or laboratory evidence of acute HIV infection, continuing antiretroviral therapy for >28 days might be prudent because such early treatment (no longer prophylaxis) might slow the progression of HIV disease. Patients with acute HIV infection should be transferred to the care of HIV treatment specialists.

In addition, clinicians who provide nPEP should monitor liver function, renal function, and hematologic parameters as indicated by the prescribing information found in antiretroviral treatment guidelines, package inserts, and the Physician's Desk Reference (see Table 3 in the original guideline document). Unusual or severe toxicities from antiretroviral drugs should be reported to the manufacturer or FDA.

HIV Prevention Counseling

The majority of persons who seek care after a possible HIV exposure do so because of failure to initiate or maintain effective risk-reduction behaviors. Notable exceptions are sexual assault survivors and children with community-acquired needlestick injuries.

Although nPEP might reduce the risk for HIV infection, it is not believed to be 100% effective. Therefore, patients should practice protective behaviors with sex partners (e.g., abstinence or consistent use of male condoms) or drug-use partners (e.g., avoidance of shared injection equipment) throughout the course of nPEP to avoid transmission to others if they become infected, and after nPEP to avoid future HIV exposures.

At follow-up visits, clinicians should assess their patients' needs for behavioral intervention, education, and services. This assessment should include frank, nonjudgmental questions about sexual behaviors, alcohol use, and illicit drug use. Clinicians should help patients identify ongoing risk issues and develop plans for improving their use of protective behaviors.

To help patients obtain indicated interventions and services, clinicians should be aware of local resources for high-quality HIV education and ongoing behavioral risk reduction, counseling and support, inpatient and outpatient alcohol and drug treatment services, substance/drug abuse treatment programs, family and mental health counseling services, and support programs for HIV-infected persons. Information about publicly funded HIV prevention programs can be obtained from state or local health departments.

Management of Source Persons

When source persons are seen during the course of evaluating a patient for potential HIV exposure, clinicians should also assess the source-person's access to relevant medical care, behavioral intervention, and social support services. If needed care cannot be provided directly, clinicians should help source persons obtain care in the community.

If a new diagnosis of HIV infection is made or evidence of other sexually transmitted infection is identified, the patient should be assisted in notifying their sexual and drug-use contacts. Assistance with confidential partner notification (without revealing the patient's identity) is available through local health departments.

Reporting and Confidentiality

Because of the emotional, social, and potential financial consequences of possible HIV infection, clinicians should handle nPEP evaluations with the highest level of confidentiality. Confidential reporting of sexually transmitted infections and newly diagnosed HIV infections to health departments should take place as dictated by local law and regulations.

For cases of sexual assault, clinicians should document their findings and assist patients with notifying local authorities. HIV test results should be recorded separately from the findings of the sexual assault examination to protect patients'

confidentiality in the event that medical records are later released for legal proceedings. Certain states and localities have special programs to provide reimbursement for medical therapy, including antiretroviral medication after sexual assault, and these areas might have specific reporting requirements. When the sexual abuse of a child is suspected or documented, the clinician should report it in compliance with state and local law and regulations.

Considerations for Vulnerable Populations

Pregnant Women and Women of Childbearing Potential

Considerable experience has been gained in recent years in the safe and appropriate use of antiretroviral medications during pregnancy, either for the benefit of the HIV-infected woman's health or to prevent transmission to newborns. To facilitate the selection of antiretroviral medications likely to be both effective and safe for the developing fetus, clinicians should consult Department of Health and Human Services (DHHS) guidelines before prescribing nPEP for a woman who is or might be pregnant.

Because of potential teratogenicity, efavirenz should not be used in any nPEP regimen during pregnancy or among women of childbearing age at risk for becoming pregnant during the course of antiretroviral prophylaxis (see Table 3 in the original guideline document). A protease inhibitor- or nucleoside reverse transcriptase inhibitor-based regimen should be considered in these circumstances. When efavirenz is prescribed to women of childbearing potential, they should be instructed about the need to avoid pregnancy. Because the effect of efavirenz on hormonal contraception is unknown, women using such contraception should be informed of the need to use an additional method (e.g., barrier contraception). In addition, because of reports of maternal and fetal mortality attributed to lactic acidosis associated with prolonged use of d4T in combination with ddI in HIV-infected pregnant women, this combination is not recommended for use in an nPEP regimen.

Children

Potential HIV exposures in children occur most often by accident (e.g., needlesticks in the community, fights, or playground incidents resulting in bleeding by an HIV-infected child) or by sexual abuse or assaults. In a review of charts from 1 year in the pediatric emergency department of one hospital, 10 children considered for nPEP were identified (six because of sexual assault and four because of needlestick injury). Eight began taking nPEP, but only two completed the 4-week course. An analysis of 9,136 reported acquired immunodeficiency syndrome cases in children identified 26 who were sexually abused with confirmed or suspected exposure to HIV infection.

The American Academy of Pediatrics has issued nPEP guidelines for pediatric patients. In addition, DHHS pediatric antiretroviral treatment guidelines provide information about the use of antiretroviral agents in children. For young children who cannot swallow capsules or tablets and to ensure appropriate dosing for drugs that do not have capsule/tablet formulations that allow pediatric dosing, drugs for which pediatric formulations are available might need to be prescribed (see Table 3 in the original guideline document). Adherence to the prescribed

medications will depend on the involvement of, and support provided to, parents or guardians.

Sexual Assault Survivors

Use of nPEP for sexual assault survivors has been widely encouraged both in the United States and elsewhere. Sexual assault is relatively common among women: 13% of a national sample of adult women reported having ever been raped (60% before age 18), and 5% reported having been raped more than once. Sexual assault is not uncommon among men. In one series from an emergency department, 5% of reported rapes involved men sexually assaulted by men. Males accounted for 11.6% of rapes reported among persons aged $\geq$12 years who responded to the National Crime Victimization Survey in 1999. However, only three documented cases of HIV infection resulting from sexual assault have been published. In observational studies, HIV infections have been temporally associated with sexual assault.

Studies have examined HIV infection rates for sexual assailants. The largest of these, an evaluation of men incarcerated in Rhode Island, determined that 1% of those convicted of sexual assault were HIV infected when they entered prison, compared with 3% of all prisoners and 0.3% of the general male population.

Sexual assault typically has multiple characteristics that increase the risk for HIV transmission if the assailant is infected. In one prospective study of 1,076 sexual assault cases, 20% were attacked by multiple assailants, 39% were assaulted by strangers, 83% of females were vaginally penetrated, and 17% overall were sodomized. Genital trauma was documented in 53% of those assaulted, and sperm or semen was detected in 48%. In another study, in which toluidine blue dye was used as an adjunct to naked-eye examination, 40% of assaulted women (70% of nulliparas) had detectable vaginal lacerations, compared with 5% of women examined after consensual sex.

Despite these risks and the establishment of multidisciplinary support services, sexual assault survivors often decline nPEP, and many who do take it do not complete the 28-day course. This pattern has been reported in several countries and several programs in North America. In Vancouver, 71 of 258 assault survivors accepted the 5-day starter pack of nPEP, 29 returned for additional doses, and eight completed 4 weeks of therapy. Those with the highest risk for HIV exposure (i.e., source known to be HIV infected, a homosexual or bisexual man, or an injection-drug user) were more likely to begin and complete nPEP.

Patients who have been sexually assaulted will benefit from supportive services to improve adherence to nPEP if it is prescribed, and from psychological and other support provided by sexual assault crisis centers. All sexually assaulted patients should be tested and administered prophylaxis for sexually transmitted infections, and women who might become pregnant should be offered emergency contraception.

Inmates

Certain illegal behaviors that result in imprisonment (e.g., prostitution and injection-drug use) also might be associated with a higher prevalence of HIV

infection among prison inmates than among the general population. However, studies indicate that the risk for becoming infected in prison is probably less than the risk outside prison. However, when exposure does occur, because sexual contact and injection-drug use are prohibited in jails and prisons, prisoners who have experienced such exposures might be unable or unwilling to report the behaviors to health-care providers.

Administrators and health-care providers working in correctional settings should develop and implement systems to make HIV education and risk-reduction counseling, nPEP, voluntary HIV testing, and HIV care confidentially available to inmates. Such programs will allow inmates to benefit from nPEP when indicated, facilitate treatment services for those with drug addiction, and assist in the identification and treatment of sexual assault survivors.

Injection-Drug Users

A history of injection-drug use should not deter clinicians from prescribing nPEP if the exposure provides an opportunity to reduce the risk for consequent HIV infection. A survey of clinicians serving injection-drug users determined a high degree of willingness to provide nPEP after different types of potential HIV exposure.

In judging whether exposures are isolated, episodic, or ongoing, clinicians should consider that persons who continue to engage in risk behaviors (e.g., commercial sex workers or users of illicit drugs) might be practicing risk reduction (e.g., using condoms with every client, not sharing syringes, and using a new sterile syringe for each injection). Therefore, a high-risk exposure might represent an exceptional occurrence for such persons despite their ongoing risk behavior.

Injection-drug users should be assessed for their interest in substance abuse treatment and their knowledge and use of safe injection and sex practices. Patients desiring substance abuse treatment should be referred for such treatment. Persons who continue to inject or who are at risk for relapse to injection-drug use should be instructed in the use of a new sterile syringe for each injection and the importance of avoiding the sharing of injection equipment. In areas where programs are available, health-care providers should refer such patients to appropriate sources of sterile injection equipment.

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for evaluation and treatment of possible nonoccupational human immunodeficiency virus (HIV) exposures.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accumulated data from animal and human clinical and observational studies demonstrate that antiretroviral therapy initiated as soon as possible within 48-72 hours of sexual, injection-drug use, and other substantial nonoccupational human immunodeficiency virus (HIV) exposure and continued for 28 days might reduce the likelihood of transmission.

POTENTIAL HARMS

Concerns about the potential risks from nonoccupational postexposure prophylaxis (nPEP) as a public health intervention include possible decrease in risk-reduction behaviors resulting from a perception that postexposure treatment is available, the occurrence of serious adverse effects from antiretroviral treatment in otherwise healthy persons (see Table 3 in the original guideline document), and potential selection for resistant virus (particularly if adherence is poor during the nPEP course).

CONTRAINDICATIONS

CONTRAINDICATIONS

- Because of potential teratogenicity, efavirenz should not be used in any nonoccupational postexposure prophylaxis (nPEP) regimen during pregnancy or among women of childbearing age at risk for becoming pregnant during the course of antiretroviral prophylaxis.
- Because of reports of maternal and fetal mortality attributed to lactic acidosis associated with prolonged use of stavudine (d4T) in combination with didanosine (ddI) in HIV infected pregnant women, this combination is not recommended for use in an nPEP regimen.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This report does not include any discussion of a product under investigational use. However, this report does contain discussion of certain drugs indicated for use in a nonlabeled manner and that are not Food and Drug Administration (FDA) approved for such use. Information included in these guidelines might not represent FDA approval or approved labeling for the particular products or indications being discussed. Specifically, the terms *safe* and *effective* might not be synonymous with the FDA-defined legal standards for product approval.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Smith DK, Grohskopf LA, Black RJ, Auerbach JD, Veronese F, Struble KA, Cheever L, Johnson M, Paxton LA, Onorato IM, Greenberg AE. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep 2005 Jan 21;54(RR-2):1-26. [126 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Sep 25 (revised 2005 Jan 21)

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]
Department of Health and Human Services (U.S.) - Federal Government Agency [U.S.]
Food and Drug Administration (U.S.) - Federal Government Agency [U.S.]
Health Resources and Services Administration - Federal Government Agency

[U.S.]
Public Health Service (U.S.) - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

External Consultants Meeting on Antiretroviral Therapy for Potential Nonoccupational Exposures to HIV

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Dawn K. Smith, MD, Division of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention, CDC, Atlanta, Georgia; Lisa A. Grohskopf, MD, Division of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention, CDC, Atlanta, Georgia; Roberta J. Black, PhD, National Institutes of Health; Judith D. Auerbach, PhD, National Institutes of Health; Fulvia Veronese, PhD, National Institutes of Health; Kimberly A. Struble, PharmD, Food and Drug Administration, Washington, DC; Laura Cheever, MD, Health Resources and Services Administration; Michael Johnson, MD, Health Resources and Services Administration; Lynn A. Paxton, MD, Division of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention, CDC, Atlanta, Georgia; Ida M. Onorato, MD, Division of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention, CDC, Atlanta, Georgia; Alan E. Greenberg, MD, Division of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention, CDC, Atlanta, Georgia

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The Centers for Disease Control (CDC), our planners, and our content specialists wish to disclose they have no financial interests or other relationships with the manufactures of commercial products, suppliers of commercial services, or commercial supporters.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Management of possible sexual, injecting-drug-use, or other nonoccupational exposure to HIV, including considerations related to antiretroviral therapy. Public Health Service statement. Centers for Disease Control and Prevention. MMWR Recomm Rep 1998 Sep 25;47(RR-17):1-14.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site.

Print copies: Available from the Centers for Disease Control and Prevention, National AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20850. Telephone: (800) 458-5231.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Management of possible sexual, injecting-drug-use, or other nonoccupational exposure to HIV, including considerations related to antiretroviral therapy tool for Palm OS* or Pocket PC. This download is also available for Palm OS or Pocket PC download from the AIDSinfo Web site.

The following are also available:

- The AIDSinfo drug database. Available from the AIDSinfo Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- AIDSinfo's HIV/AIDS Glossary, 4th ed. Available for PDA, in HTML format, and in Portable Document Format (English and Spanish) from the AIDSinfo Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- A comprehensive Spanish-language Web site featuring information about HIV treatment and clinical trials is available at http://aidsinfo.nih.gov/infoSIDA/.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on March 29, 1999. The information was verified by the guideline developer as of July 21, 1999. This NGC summary was updated on January 31, 2005. This summary was updated by ECRI Institute on October 2, 2007, following the U.S. Food and Drug Administration advisory on Viracept (nelfinavir mesylate). This summary was updated by ECRI Institute on August 11, 2008 following the U.S. Food and Drug Administration advisory on Ziagen (abacavir sulfate).

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